

Claims (encompassing any amendments)

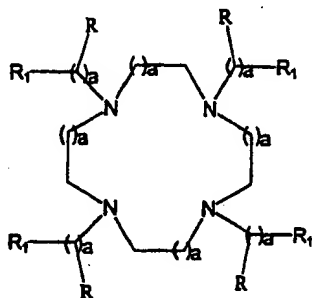
What is Claimed is:

1. (amended) A method of generating a contrast enhanced image of a human or non-human animal subject which comprises administering to said subject an effective amount of a magnetic resonance imaging contrast agent and generating an image of at least part of said subject containing said agent, wherein said agent comprises a physiologically tolerable Europium compound, preferably a chelate complex of Europium or a physiologically tolerable salt thereof having first and second oxidation states which differs in relaxivity by a factor of at least 5, and wherein said Europium compound is activated by switching between the II and III oxidation states of metal ions *in vivo* whereby contrast difference is enhanced in a body region in which conversion between the oxidation states occurs.
2. (amended) A method as claimed in claim 1 wherein said agent comprises a physiologically tolerable Europium compound or salt thereof having first and second oxidation states which differ in relaxivity by a factor of at least 10.
3. (amended) A method as claimed in claim 1 wherein said agent comprises a physiologically tolerable Europium compound or salt thereof having first and second oxidation states which differ in relaxivity by a factor of at least 20.
4. (amended) A method as claimed in claim 1 wherein said agent comprises a physiologically tolerable Europium compound or salt thereof having first and second oxidation states which differ in relaxivity by a factor of at least 100.
6. (amended) A method as claimed in claim 1 wherein said change between two paramagnetic states is effected as a change from a spherically symmetric electronic ground state to a non-spherically symmetric excited state.

10. (amended) A method as claimed in claim 1 wherein said chelate complex is a complex of a chelant selected from the group consisting of DTPA, EDTA, DTPA-BMA, DO3A, DOTA, HP-DO3A, TMT and DPDP.

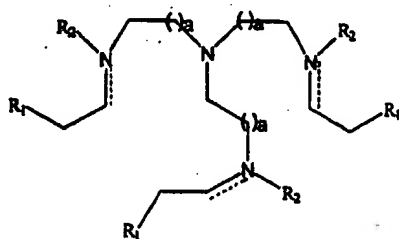
11. (amended) A method as claimed in claim 1 wherein said chelate complex is a complex of a chelant selected from the group consisting of porphyrins and porphyrin-like molecules, phthalocyanines, crown ethers, hemin, heme, chelants having a square planar symmetry, cryptands and cryptates.

12. (amended) A method as claimed in claim 1 wherein said chelate complex is a complex of a chelant selected from compounds of formulae (I), (II), (III), (IV), (V) and (VI):



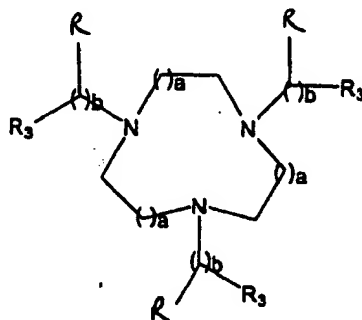
(I)

where each a independently represents an integer between 1 and 3, each R independently represents hydrogen or hydroxy and each R_1 independently represents a carboxylate, phosphate, thioacid, thiol, amino alkoxide or hydroxy group;



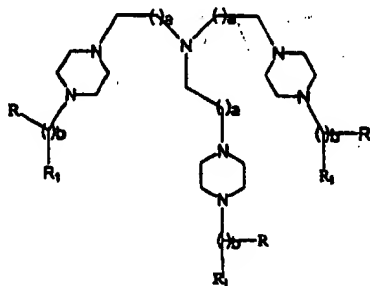
(II)

where a and R_1 are as hereinbefore defined and each R_2 independently represents hydrogen, C_{1-6} alkyl or aryl, with the proviso that R_2 is absent when the double bond is present on the same nitrogen;



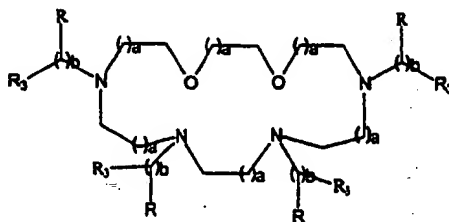
(III)

where a, R and R_2 are as hereinbefore defined, b is an integer between 0-3 and each R_3 independently represents R_1 , $NR-NR_2-COO^{\theta}$, or $N=N-COO^{\theta}$ when b is positive or each R_3 independently represents $N=CH-COO^{\theta}$ or $NR_2-CH_2-COO^{\theta}$;



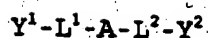
(IV)

where a, b, R and R_1 are as hereinbefore defined;



(V)

where a, b, R and R_3 are as hereinbefore defined;



(VI)

where A is N, CR₄, P, P=O, *cis,cis,cis*-1,3,5-trisubstituted-cyclohexane or an N,N',N''-trisubstituted-triaza 9 to 14 membered macrocyclic ring;

L¹,L²,L³ are linker groups which are independently chosen from C₁₋₄ alkylene, C₄₋₈ cycloalkylene or C₄₋₈ o-arylene;

Y¹,Y²,Y³ are independently chosen from -NH₂, -B(=O)OZ, -N=CR₅-B(=O)OZ, -NR₅-CR₆-B(=O)OZ, -N[CR₆-B(=O)Q]₂ and -O-CR₆-B(=O)OZ where B is C or PR₆, each Q is independently -OZ or -NR₆, and Z is H or a counter-ion;

each R₄ and R₅ group is independently chosen from H, C₁₋₅ alkyl, C₁₋₅ lkoxyalkyl, C₁₋₅ hydroxyalkyl, C₁₋₅ aminoalkyl, C₅₋₁₀ aryl or C₁₋₆ fluoroalkyl;

R₆ is OH, C₁₋₆ alkyl, C₁₋₆ alkoxyalkyl, C₁₋₆ fluoroalkyl, C₁₋₁₀ alkoxy or C₅₋₁₀ aryl; with the proviso that at least one of Y¹, Y² and Y³ is -N=CR₅-B(=O)OZ.

13. (amended) A method as claimed in claim 1 wherein said agent is conjugated to a biological vector capable of targeting said agent to a desired region of the body.

14. A method as claimed in claim 13 wherein said biological vector is selected from the group consisting of an antibody, and antibody fragment and an oligopeptide binding motif.

15. (amended) A method as claimed in claim 1 wherein conversion between said first and second oxidation states is effected *in vivo* by a localised normal or abnormal biological process, by an administered chemical agent or by illumination of said agent with light.

16. A method as claimed in claim 15 wherein conversion between said first and second oxidation states is effected *in vivo* by the presence or absence of oxygen or of oxidation or reduction promoting agents, from a change in temperature or as a result of an increase or decrease in pH at the target site, or as a result of the presence of a specific enzyme.

17. A method as claimed in claim 15 wherein said chemical agent is a redox reagent capable of delivery to or accumulation at a desired target site within the body.

18. A method as claimed in claim 15 wherein conversion between said first and second oxidation states is effected by application of light having a wavelength of from 600 to 1300 nm.

19. (amended) An MR contrast agent composition comprising as an MR contrast agent a physiologically tolerable Europium compound, preferably a chelate complex of Europium or a physiologically tolerable salt thereof having first and second oxidation states which differs in relaxivity by a factor of at least 5, and wherein said Europium compound is activated by switching between the II and III oxidation states of the metal ions *in vivo* whereby contrast difference is enhanced in a body region in which conversion between the oxidation states occurs, together with an optionally encapsulated physiologically tolerable trigger substance capable of converting said contrast agent between said first and second oxidation states.

20. A composition as claimed in claim 19 wherein said trigger substance is an enzyme, a redox agent or a free radical scavenger.